

TOBACCO INDUSTRY RESEARCH COMMITTEE
150 EAST FORTY SECOND STREET NEW YORK 17, N.Y.

#128R2

Application For Research Grant

Activated 7/1/56
Renewed 7/1/57

Date: January 24, 1958

1. Name of Investigator:

1. Paul B. Larson
2. Harvey B. Haag
3. Herbert McKennis, Jr.

2. Title:

1. Professor of Pharmacology
2. Professor of Pharmacology
3. Professor of Pharmacology

3. Institution

& Address:

Medical College of Virginia
Richmond 19, Virginia

4. Project or Subject:

Enzymatic Transformation of Nicotine and Related Compounds.

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

In the enclosed semi-annual progress report it will be seen that by means of fractional crystallization, chromatography and extraction it has been possible to identify two metabolites of nicotine and separate others. By use of these methods it is planned to investigate further the nature of the unidentified nicotine metabolites and to chemically identify these. Studies are also planned which will provide information about nicotine metabolites which do not give positive Koenig tests. It is considered that experiments with C-14 or tritium labelled nicotine will give the most satisfactory results in the search for the Koenig negative compounds. Current experiments have shown that the major portion of nicotine is metabolized to Koenig negative compounds which contain either a substituted or degraded pyridine nucleus. The radioactive compounds should, in addition to providing a satisfactory route to the uninvestigated fraction of metabolized nicotine, ~~facilitate~~ facilitate greatly studies on the role of the bile in excretion of nicotine and metabolites.

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6. Budget Plan:

Social Security		230
Salaries		16,400
Expendable Supplies		4,500
Permanent Equipment		3,485
Overhead (10%)		2,572
Other		1,100
Total		28,287

7. Anticipated Duration of Work: One year; it is intended to review the progress of the current investigation in the fall of 1958 and thereafter to make an application for extension of the grant.

8. Facilities and Staff Available:

General pharmacologic and biochemical equipment; fraction collectors, Lardy type Warburg apparatus, Refrigerated centrifuge, C^{14} counting equipment (Libby anti-coincidence counter, nuclear instrument glass flow counter with automatic sample changer) paper chromatographic equipment, polarimeter, greenhouse facilities for growing C^{14} labelled plants.

9. Additional Requirements: What if any, will depend upon how the project develops.

10. Additional Information (Including relation of work to other projects and other sources of supply):

Salary breakdown: Lemox B. Turnbull, Ph.D. \$8,400
 Edward R. Bowman, M.S. 6,200
 Lab. Assistant (part-time) 1,200
 Animal man (part-time) 600
 Social Security 230

Other-breakdown: Travel \$750

Fees for human volunteers (nicotine) 350

Permanent equipment-breakdown: Spinco Preparative Centrifuge \$2950
 (with rotors)
 Constant infusion pump 535

The centrifuge will make possible preparation of active enzymatic fractions and the pump will insure reproducibility in animal experiments.

/s/ Paul S. Larson
 /s/ Harvey B. Haag
 /s/ Herbert McKennis, Jr.
 Signature _____
 Director of Project

/s/ V. E. Franklin
 Business Officer of the Institution

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